Serial No.: 10/598,520

Filed: December 7, 2007

Page : 2 of 36

## AMENDMENTS TO THE CLAIMS

The following listing of claims replaces all prior versions and listings of claims in the application.

## **Listing of Claims**

1. (currently amended) A <u>pharmaceutical composition comprising a compound of the following general formula, or a pharmaceutically acceptable salt thereof, for use as a medicament:</u>

$$R_{6}$$
 $R_{1}$ 
 $R_{5}$ 
 $R_{1}$ 

or a pharmaceutically acceptable salt thereof;

and a physiologically acceptable carrier, excipient or diluent;

wherein the pharmaceutical composition is suitable for human therapeutic administration; and

wherein:

(I) when X [[=]] is OH, R<sub>2</sub> [[=]] is NH<sub>2</sub>, R<sub>5</sub> [[=]] is CH<sub>2</sub>OH, R<sub>6</sub> [[=]] is H, and R<sub>1</sub> is C<sub>5</sub>-C<sub>6</sub> alkoxy, OCH<sub>2</sub>Cyclopropyl, OCH<sub>2</sub>Cyclopentyl, O-(2,2,3,3-tetrafluorocycloButyl), phenoxy, substituted phenoxy, OCH<sub>2</sub>CH<sub>2</sub>OH, or OCH<sub>2</sub>CHF<sub>2</sub>, (5-indanyl)oxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>5</sub>, or C<sub>6</sub> alkylamino, (R) or (S)-sec-Butylamino, C<sub>5</sub> or C<sub>6</sub> cycloalkylamino, exo-norbornane amino, N-methyl-N-isoamylamino(N-methyl, N-isoamylamino), phenylamino, phenylamino with either a methoxy substituent or a fluoro

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 3 of 36

substituent[[s]], a C<sub>2</sub> sulfone group, a C<sub>7</sub> alkyl group, a cyano group, a CONH<sub>2</sub> group, or 3,5-dimethylphenyl; or

when X = [=] is H,  $R_2 = [=] is NH_2$ ,  $R_5 = [=] is CH_2OH$ ,  $R_6 = [=] is H$ , and  $R_1 is n$ -hexyloxy.; or

(II) when X = OH, R<sub>1</sub> = H, R<sub>5</sub> = CH<sub>2</sub>OH, R<sub>6</sub> = H, R<sub>2</sub> is NMe<sub>2</sub>, N-(2-isopentenyl), piperazinyl, (N-Me, N-benzyl), (N-Me, N-CH<sub>2</sub>Ph(3-Br)), (N-Me, N-CH<sub>2</sub>Ph(3-CF<sub>3</sub>)), or (N-Me, N-(2-methoxyethyl)), or OCH<sub>2</sub>Cyclopentyl; or

(III) when X = OH,  $R_5 = CONHR_3$ ,  $R_6 = H$ :

R<sub>1</sub> is H, R<sub>3</sub> is an isopropyl group, and R<sub>2</sub> is either NH<sub>2</sub> or a methylamino group (NHMe) or an isoamyl group (CH<sub>2</sub>CH<sub>2</sub>CHMe<sub>2</sub>); or

R<sub>1</sub> is H, R<sub>3</sub> is H, and R<sub>2</sub> is NH<sub>2</sub>; or

R<sub>1</sub> is OMe, R<sub>3</sub> is Ph, and R<sub>2</sub> is NH<sub>2</sub>; or

R<sub>1</sub>-is NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Me, R<sub>3</sub> is CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Me, and R<sub>2</sub> is NH<sub>2</sub>; or

(IV) when X = OH,  $R_1 = H$ ,  $R_2 = NH_2$ ,  $R_5 = CH_2NHCOR_4$ ,  $R_6 = H$ ,  $R_4$  is *n*-propyl or  $NHCH_2CH_3$ ; or

(V) when X = OH,  $R_5 = CH_2OH$ ,  $R_6 = H$ :

R<sub>1</sub> is NHCyclohexyl when R<sub>2</sub> is NMe<sub>2</sub>; or

R<sub>1</sub> is OMe when R<sub>2</sub> is NHBenzyl; or

(VI) when X = OH,  $R_2 = NH_2$ ,  $R_5 = CH_2OH$ ,  $R_6 = Me$ ,  $R_1$  is NHCyclohexyl, NHCyclopentyl, or NH-n-Hexyl.

- 2. (currently amended) A <u>composition</u><del>compound</del> according to formula (I) of claim 1, or a pharmaceutically acceptable salt thereof, for use as a medicament, wherein when X is OH, R<sub>2</sub> is NH<sub>2</sub>, R<sub>5</sub> is CH<sub>2</sub>OH, and R<sub>6</sub> is H, R<sub>1</sub> is phenoxy substituted with 4-nitrile, 4-methyl, 3-phenyl, 3-bromo, 3-isopropyl, 2-methyl, 2,4-difluoro, 2,5-difluoro, 3,4-difluoro, 2,3,5-trifluoro, or (3-methyl,4-fluoro).
- 3. (currently amended) A <u>composition compound</u> according to claim 1, with a structure as defined in any of Examples 1-6 wherein the compound is a compound selected from the

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 4 of 36

group consisting of compound numbers 2-3 and 5-40 as defined below, or a pharmaceutically acceptable salt of such a compound: thereof, for use as a medicament

| Compound      | <u>X</u>  | D.  |
|---------------|-----------|---|
| <u>Number</u> | <u> </u>  | $\underline{\mathbf{R}_1}$  |
| 2             | <u>OH</u> | OCH <sub>2</sub> CHF <sub>2</sub>   |
| 3             | <u>OH</u> | OCH <sub>2</sub> Cyclopropyl  |
| <u>5</u>      | <u>OH</u> | O CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> |
| <u>6</u>      | <u>OH</u> | <u>OPh</u>  |
| 7             | <u>OH</u> | O-(4-cyano)Ph   |
| 8             | <u>OH</u> | O-(3-Ph)Ph  |
| 9             | <u>OH</u> | O-(2,5-F <sub>2</sub> )Ph   |
| 10            | <u>OH</u> | O-(2,4-F <sub>2</sub> )Ph   |
| 11            | <u>OH</u> | O-(3,4-F <sub>2</sub> )Ph   |
| 12            | <u>OH</u> | O-(2,3,5-F <sub>3</sub> )Ph   |
| <u>13</u>     | <u>OH</u> | O-(3-Me, 4-F)Ph   |
| 14            | <u>OH</u> | <u>O-(2-Me)Ph</u>   |
| 15            | <u>OH</u> | <u>O-(3-Br)Ph</u>   |
| <u>16</u>     | <u>OH</u> | <u>O-(4-Me)Ph</u>   |
| <u>17</u>     | <u>OH</u> | <u>5-indanyloxy</u>   |
| 18            | OH        | O-(3-CH(CH <sub>3</sub> ) <sub>2</sub> )Ph  |
| <u>19</u>     | <u>OH</u> | NHCH <sub>3</sub>   |
| <u>20</u>     | OH        | NHCH <sub>2</sub> CH <sub>3</sub>   |

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 5 of 36

| Compound Number | X         | $\underline{\mathbf{R_1}}$  |
|-----------------|-----------|---|
| <u>21</u>       | OH        | N(CLL)  |
|                 |           | N(CH <sub>3</sub> ) <sub>2</sub>  |
| <u>22</u>       | <u>OH</u> | NH-(R)-sec-Butyl  |
| <u>23</u>       | <u>OH</u> | NH-(S)-sec-Butyl  |
| 24              | <u>OH</u> | NHCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> |
| <u>25</u>       | <u>OH</u> | NH-exo-norbornane   |
| <u>26</u>       | <u>OH</u> | NHPh  |
| <u>27</u>       | <u>OH</u> | NH-(4-MeO)Ph  |
| <u>28</u>       | <u>OH</u> | <u>NH-(4-F)Ph</u>   |
| <u>29</u>       | <u>OH</u> | NH-cyclopentyl  |
| 30              | <u>OH</u> | NH-cyclohexyl   |
| 31              | <u>OH</u> | N(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> CH(CH <sub>3</sub> ) <sub>2</sub>              |
| <u>32</u>       | OH        | OCH <sub>2</sub> cyclopentyl  |
| <u>33</u>       | <u>OH</u> | SO <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>   |
| <u>34</u>       | <u>OH</u> | OCH <sub>2</sub> CH <sub>2</sub> OH   |
| 35              | OT.       | O-(2,2,3,3-tetrafluoro-   |
| 33              | <u>OH</u> | cycloButyl)   |
| <u>36</u>       | <u>OH</u> | CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>   |
| <u>37</u>       | <u>OH</u> | 3,5-Me <sub>2</sub> -Phenyl   |
| 38              | <u>OH</u> | <u>CN</u>   |
| <u>39</u>       | <u>OH</u> | <u>CONH</u> <sub>2</sub>  |
| 40              | H         | O CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> |

4. (currently amended) A <u>composition compound</u> according to claim 3, <u>wherein the compound is a compound selected from the group consisting of with a structure corresponding to any of compound numbers 2, 3, 7-19, 22-25, 28, 31-33, <u>and or 35-40 60</u> as defined <u>belowin Examples 1-6</u>, or a pharmaceutically acceptable salt <u>of such a compound:thereof, for use as a medicament.</u></u>

Applicant: Martyn Pritchard et al. Serial No.: 10/598,520 Attorney's Docket No.: 13425-0200US1/BV-1093 US

: December 7, 2007 : 6 of 36 Filed

Page

$$\frac{N}{N}$$
 $\frac{N}{N}$ 
 $\frac{N}$ 

| Compound Number | <u>X</u>  | $\underline{\mathbf{R_1}}$                 |
|-----------------|-----------|--|
| 2               | <u>OH</u> | OCH <sub>2</sub> CHF <sub>2</sub>          |
| <u>3</u>        | <u>OH</u> | OCH <sub>2</sub> Cyclopropyl               |
| 7               | <u>OH</u> | O-(4-cyano)Ph                              |
| 8               | ОН        | O-(3-Ph)Ph                                 |
| 9               | <u>OH</u> | O-(2,5-F <sub>2</sub> )Ph                  |
| 10              | <u>OH</u> | O-(2,4-F <sub>2</sub> )Ph                  |
| 11              | OH        | O-(3,4-F <sub>2</sub> )Ph                  |
| <u>12</u>       | <u>OH</u> | O-(2,3,5-F <sub>3</sub> )Ph                |
| <u>13</u>       | <u>OH</u> | O-(3-Me, 4-F)Ph                            |
| 14              | <u>OH</u> | <u>O-(2-Me)Ph</u>                          |
| <u>15</u>       | <u>OH</u> | <u>O-(3-Br)Ph</u>                          |
| <u>16</u>       | OH        | <u>O-(4-Me)Ph</u>                          |
| <u>17</u>       | <u>OH</u> | <u>5-indanyloxy</u>                        |
| 18              | <u>OH</u> | O-(3-CH(CH <sub>3</sub> ) <sub>2</sub> )Ph |
| <u>19</u>       | <u>OH</u> | NHCH <sub>3</sub>                          |
| <u>22</u>       | OH        | NH-(R)-sec-Butyl                           |
| 23              | <u>OH</u> | NH-(S)-sec-Butyl                           |
| 24              | <u>OH</u> | NHCH2CH2CH2CH2CH3                          |
| <u>25</u>       | <u>OH</u> | NH-exo-norbornane                          |
| 28              | <u>OH</u> | <u>NH-(4-F)Ph</u>                          |

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 7 of 36

| Compound      | X         | $\underline{\mathbf{R_1}}$  |
|---------------|-----------|---|
| <u>Number</u> |           | <u> </u>  |
| <u>31</u>     | <u>OH</u> | N(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> CH(CH <sub>3</sub> ) <sub>2</sub>              |
| 32            | <u>OH</u> | OCH <sub>2</sub> cyclopentyl  |
| <u>33</u>     | <u>OH</u> | SO <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>   |
| <u>35</u>     | <u>OH</u> | O-(2,2,3,3-tetrafluoro-   |
| <u>55</u>     | <u> </u>  | cycloButyl)   |
| <u>36</u>     | <u>OH</u> | CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>   |
| <u>37</u>     | <u>OH</u> | 3,5-Me <sub>2</sub> -Phenyl   |
| 38            | <u>OH</u> | CN  |
| <u>39</u>     | OH        | <u>CONH</u> <sub>2</sub>  |
| 40            | H         | O CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> |

5. (currently amended) A <u>composition compound</u> according to claim 3, <u>wherein the compound is a compound selected from the group consisting of with a structure corresponding to any of compound numbers 2, 3, 7-18, 22-25, 31-33, 35, 37, <u>and 40, 44, 45, 47, 48, or 51-60</u> as defined <u>belowin Examples 1-6</u>, or a pharmaceutically acceptable salt <u>of such a compound:thereof, for use as a medicament.</u></u>

| <u>Compound</u><br><u>Number</u> | X         | $\underline{\mathbf{R_1}}$        |
|----------------------------------|-----------|-----------------------------------|
| 2                                | <u>OH</u> | OCH <sub>2</sub> CHF <sub>2</sub> |
| <u>3</u>                         | <u>OH</u> | OCH <sub>2</sub> Cyclopropyl      |

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 8 of 36

| Compound      | Y          | <b>D</b> .  |
|---------------|------------|---|
| <u>Number</u> | X          | $\underline{\mathbf{R_1}}$  |
| 7             | <u>OH</u>  | O-(4-cyano)Ph   |
| 8             | <u>OH</u>  | <u>O-(3-Ph)Ph</u>   |
| 9             | OH         | O-(2,5-F <sub>2</sub> )Ph   |
| 10            | OH         | O-(2,4-F <sub>2</sub> )Ph   |
| 11            | OH         | O-(3,4-F <sub>2</sub> )Ph   |
| 12            | OH         | O-(2,3,5-F <sub>3</sub> )Ph   |
| <u>13</u>     | <u>OH</u>  | O-(3-Me, 4-F)Ph   |
| 14            | <u>OH</u>  | <u>O-(2-Me)Ph</u>   |
| 15            | <u>OH</u>  | <u>O-(3-Br)Ph</u>   |
| <u>16</u>     | OH         | <u>O-(4-Me)Ph</u>   |
| 17            | OH         | 5-indanyloxy  |
| 18            | <u>OH</u>  | O-(3-CH(CH <sub>3</sub> ) <sub>2</sub> )Ph  |
| 22            | <u>OH</u>  | NH-(R)-sec-Butyl  |
| 23            | <u>OH</u>  | NH-(S)-sec-Butyl  |
| 24            | <u>OH</u>  | NHCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> |
| <u>25</u>     | OH         | NH-exo-norbornane   |
| 31            | <u>OH</u>  | N(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> CH(CH <sub>3</sub> ) <sub>2</sub>              |
| 32            | <u>OH</u>  | OCH <sub>2</sub> cyclopentyl  |
| 33            | <u>OH</u>  | SO <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>   |
| 35            | OH         | O-(2,2,3,3-tetrafluoro-   |
| <u> </u>      | OII        | cycloButyl)   |
| 37            | <u>OH</u>  | 3,5-Me <sub>2</sub> -Phenyl   |
| 40            | · <u>H</u> | O CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> |

## 6-28 (cancelled)

29. (currently amended) A <u>composition compound</u> according to claim 3, <u>wherein the</u> <u>compound is a compound selected from the group consisting of with a structure</u>

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 9 of 36

corresponding to any of compound numbers 2, 3, 7-13, 15, 17, 18, 22-25, 31-33, 35, 37, and 40, 44, 45, 47, 48, or 51-60 as defined belowin Examples 1-6, or a pharmaceutically acceptable salt of such a compound: thereof.

$$R_1$$

| <u>Compound</u><br><u>Number</u> | $\underline{\mathbf{X}}$ | $\underline{\mathbf{R}_1}$  |
|----------------------------------|--------------------------|---|
| 2                                | <u>OH</u>                | OCH <sub>2</sub> CHF <sub>2</sub>   |
| 3                                | OH                       | OCH <sub>2</sub> cyclopropyl  |
| <u>5</u>                         | <u>OH</u>                | O CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> |
| 7                                | OH                       | O-(4-cyano)Ph   |
| 8                                | <u>OH</u>                | <u>O-(3-Ph)Ph</u>   |
| 9                                | <u>OH</u>                | O-(2,5-F <sub>2</sub> )Ph   |
| 10                               | <u>OH</u>                | <u>O-(2,4-F<sub>2</sub>)Ph</u>  |
| 11                               | <u>OH</u>                | O-(3,4-F <sub>2</sub> )Ph   |
| 12                               | <u>OH</u>                | O-(2,3,5-F <sub>3</sub> )Ph   |
| 13                               | <u>OH</u>                | O-(3-Me, 4-F)Ph   |
| <u>15</u>                        | <u>OH</u>                | <u>O-(3-Br)Ph</u>   |
| <u>17</u>                        | OH                       | 5-indanyloxy  |
| <u>18</u>                        | <u>OH</u>                | O-(3-CH(CH <sub>3</sub> ) <sub>2</sub> )Ph  |
| 22                               | <u>OH</u>                | NH-(R)-sec-Butyl  |
| 23                               | <u>OH</u>                | NH-(S)-sec-butyl  |
| 24                               | <u>OH</u>                | NHCH2CH2CH2CH2CH3   |
| <u>25</u>                        | <u>OH</u>                | NH-exo-norbornane   |

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 10 of 36

| Compound Number | X         | $\underline{\mathbf{R_1}}$  |
|-----------------|-----------|---|
| <u>31</u>       | <u>OH</u> | N(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> CH(CH <sub>3</sub> ) <sub>2</sub>              |
| <u>32</u>       | <u>OH</u> | OCH <sub>2</sub> cyclopentyl  |
| <u>33</u>       | <u>OH</u> | SO <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>   |
| <u>35</u>       | <u>OH</u> | O-(2,2,3,3-tetrafluoro-<br>cyclobutyl)  |
| <u>37</u>       | <u>OH</u> | 3,5-Me <sub>2</sub> -Phenyl   |
| <u>40</u>       | H         | O CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> |

- 30. (withdrawn, currently amended) A method of preventing, treating, or ameliorating a pathological condition that can be prevented or improved by agonism of adenosine A2A receptors, which comprises administering a compound composition as defined in claim 1 to a subject in need of such prevention, treatment, or amelioration.
- 31 (cancelled)
- 32. (withdrawn, currently amended) A method of preventing, treating, or ameliorating pain which comprises administering a compound composition as defined in claim 1 to a subject in need of such prevention, treatment, or amelioration.
- 33. (withdrawn, currently amended) A method of preventing, treating, or ameliorating ischaemic pain which comprises administering a compound composition as defined in claim 1 to a subject in need of such prevention, treatment, or amelioration.
- 34. (withdrawn) A method according to claim 33 for the prevention, treatment, or amelioration of ischaemic pain associated with coronary artery disease, peripheral artery disease, left ventricular hypertrophy, essential hypertension, acute hypertensive emergency, cardiomyopathy, heart insufficiency, exercise tolerance, chronic heart failure, arrhythmia, cardiac dysrhythmia, syncopy, arteriosclerosis, mild chronic heart failure, angina pectoris, Prinzmetal's (variant) angina, stable angina, exercise induced angina,

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 11 of 36

cardiac bypass reocclusion, intermittent claudication (arteriosclerosis oblitterens), arteritis, diastolic dysfunction, systolic dysfunction, atherosclerosis, post ischaemia/reperfusion injury, diabetes (Types I or II), thromboembolisms, haemorrhagic accidents, or neuropathic or inflammatory pain arising from hypoxia-induced nerve cell damage.

- 35. (withdrawn, currently amended) A method of prevention, treatment, or amelioration of inflammation, which comprises administering a compound composition as defined in claim 1 to a subject in need of such prevention, treatment, or amelioration.
- 36. (withdrawn) A method according to claim 35 for the prevention, treatment, or amelioration of inflammation caused by or associated with: cancer (such as leukemias, lymphomas, carcinomas, colon cancer, breast cancer, lung cancer, pancreatic cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic, lung, breast, and prostate metastases, etc.); auto-immune disease (such as organ transplant rejection, lupus erythematosus, graft v. host rejection, allograft rejections, multiple sclerosis, rheumatoid arthritis, type I diabetes mellitus including the destruction of pancreatic islets leading to diabetes and the inflammatory consequences of diabetes); autoimmune damage (including multiple sclerosis, Guillam Barre Syndrome, myasthenia gravis); obesity; cardiovascular conditions associated with poor tissue perfusion and inflammation (such as atheromas, atherosclerosis, stroke, ischaemia-reperfusion injury, claudication, congestive heart failure, vasculitis, haemorrhagic shock, vasospasm following subarachnoid haemorrhage, vasospasm following cerebrovascular accident, pleuritis, pericarditis, the cardiovascular complications of diabetes); ischaemia-reperfusion injury, ischaemia and associated inflammation, restenosis following angioplasty and inflammatory aneurysms; epilepsy, neurodegeneration (including Alzheimer's Disease), muscle fatigue or muscle cramp (particularly athletes' cramp), arthritis (such as rheumatoid arthritis, osteoarthritis, rheumatoid spondylitis, gouty arthritis), fibrosis (for example of the lung, skin and liver), sepsis, septic shock, encephalitis, infectious arthritis, Jarisch-Herxheimer reaction, shingles, toxic shock, cerebral malaria, Lyme's disease,

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 12 of 36

endotoxic shock, gram negative shock, haemorrhagic shock, hepatitis (arising both from tissue damage or viral infection), deep vein thrombosis, gout; conditions associated with breathing difficulties (e.g. chronic obstructive pulmonary disease, impeded and obstructed airways, bronchoconstriction, pulmonary vasoconstriction, impeded respiration, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcosis, cystic fibrosis, pulmonary hypertension, pulmonary vasoconstriction, emphysema, bronchial allergy and/or inflammation, asthma, hay fever, rhinitis, vernal conjunctivitis and adult respiratory distress syndrome); conditions associated with inflammation of the skin (including psoriasis, eczema, ulcers, contact dermatitis); conditions associated with inflammation of the bowel (including Crohn's disease, ulcerative colitis and pyresis, irritable bowel syndrome, inflammatory bowel disease); HIV (particularly HIV infection), bacterial meningitis, TNF-enhanced HIV replication, TNF inhibition of AZT and DDI activity, osteoporosis and other bone resorption diseases, osteoarthritis, rheumatoid arthritis, infertility from endometriosis, fever and myalgia due to infection, cachexia secondary to cancer, cachexia secondary to infection or malignancy, cachexia secondary to acquired immune deficiency syndrome (AIDS), AIDS related complex (ARC), keloid formation, scar tissue formation, adverse effects from amphotericin B treatment, adverse effects from interleukin-2 treatment, adverse effects from OKT3 treatment, or adverse effects from GM-CSF treatment, and other conditions mediated by excessive anti-inflammatory cell (including neutrophil, eosinophil, macrophage and Tcell) activity.

37. (withdrawn, currently amended) A method of preventing, treating, or ameliorating macro or micro vascular complications of type 1 and 2 diabetes, retinopathy, nephropathy, autonomic neuropathy, or blood vessel damage caused by ischaemia or atherosclerosis which comprises administering a compound composition as defined in claim 1 to a subject in need of such prevention, treatment, or amelioration.

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 13 of 36

38. (withdrawn, currently amended) A method of slowing the progression of arthropathy, which comprises administering a compound composition as defined in claim 1 as a disease-modifying antirheumatic drug (DMARD) to a subject in need thereof.

- 39. (withdrawn) A method according to claim 38, for slowing the progression of rheumatoid arthritis.
- 40. (withdrawn, currently amended) A method according to claim 30, wherein the eompound composition is administered at a dose that gives rise to a peak plasma concentration of the compound that is less than the EC50 value of the compound at adenosine receptors at pH 7.4.
- 41. (withdrawn, currently amended) A method according to claim 30, wherein the eompound composition is administered to the subject in an amount that results in a peak plasma concentration of the compound in the subject that is one ten thousandth to one half of the lowest EC50 value of the compound at adenosine receptors.
- 42. (withdrawn, currently amended) A method according to claim 30, wherein the compound composition is administered to the subject in an amount that results in a plasma concentration of the compound in the subject being maintained for more than one hour at one ten thousandth to one half of the lowest EC50 value of the compound at adenosine receptors.
- (withdrawn, currently amended) A method according to claim 30, wherein the eompound composition is administered to the subject in an amount that results in a peak plasma concentration of the compound in the subject that is one ten thousandth to one half of the lowest Kd value of the compound at adenosine receptors.
- 44. (withdrawn, currently amended) A method according to claim 30, wherein the compound composition is administered to the subject in an amount that results in a plasma concentration of the compound in the subject being maintained for more than one hour at

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 14 of 36

one ten thousandth to one half of the lowest Kd value of the compound at adenosine receptors.

- 45. (withdrawn, currently amended) A method according to claim 30, wherein the compound composition is administered to the subject in an amount that is one ten thousandth to one half of the minimum amount of the compound that gives rise to bradycardia, hypotension or tachycardia side effects in animals of the same species as the subject to which the compound is administered.
- (withdrawn, currently amended) A method according to claim 30, wherein the compound composition is administered at a dose that is one thousandth to one half of the minimum dose of the compound that gives rise to bradycardia, hypotension or tachycardia side effects in animals of the same species as the subject to which the dose is to be administered.
- 47. (withdrawn) A method according to claim 46, wherein the dose is one hundredth to one half of the minimum dose that gives rise to the side effects.
- (withdrawn, currently amended) A method according to claim 30, wherein the eompound composition is administered to the subject in an amount that results in a plasma concentration of the compound in the subject being maintained for more than one hour at one ten thousandth to one half of the minimum plasma concentration of the compound that gives rise to bradycardia, hypotension or tachycardia side effects in animals of the same species as the subject to which the compound is administered.
- 49. (withdrawn, currently amended) A method according to claim 30, wherein the compound composition is administered at a dose that results in a plasma concentration of the compound that is maintained for more than one hour between one hundredth and one half of the minimum dose of the compound that gives rise to bradycardia, hypotension or tachycardia side effects in animals of the same species as the subject to which the compound is to be administered.

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 15 of 36

(withdrawn, currently amended) A method according to claim 30, wherein the compound composition is administered at in an amount which provides a dose of the compound of less than 0.4mg/kg.

- (withdrawn, currently amended) A method according to claim 30, wherein the compound composition is administered at in an amount which provides a dose[[age]] of the compound of 0.001 to 0.4mg/kg.
- 52. (withdrawn, currently amended) A method according to claim 30, wherein the compound composition is administered at in an amount which provides a dose of the compound of at least 0.003mg/kg.
- 53. (withdrawn, currently amended) A method according to claim 30, wherein the compound composition is administered at in an amount which provides a dose of the compound of 0.01 to 0.1mg/kg.
- (withdrawn, currently amended) A method according to claim 30, wherein the compound composition is administered orally, parenterally, sublingually, transdermally, intrathecally, transmucosally, intravenously, intramuscularly, subcutaneously, topically, or by inhaling.
- 55. (withdrawn, currently amended) A method according to claim 30, wherein the compound composition is administered at a frequency of 2 or 3 times per day.
- 56. (withdrawn) A method according to claim 30, wherein the subject is a human subject.
- 57. (cancelled)
- 58. (previously presented) A pharmaceutical composition in unit dose form comprising up to 500mg of a compound as defined in claim 1, excluding 2-phenylamino adenosine, and a physiologically acceptable carrier, excipient, or diluent.

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 16 of 36

59. (withdrawn) A pharmaceutical composition in unit dose form comprising up to 500mg of a compound as defined in claim 1 together with an NSAID or a DMARD, and a physiologically acceptable carrier, excipient, or diluent.

60-76 (cancelled)

77. (new) A compound of the following general formula:

$$R_{6}$$
 $R_{1}$ 
 $R_{5}$ 
 $R_{1}$ 
 $R_{1}$ 

or a pharmaceutically acceptable salt thereof; wherein:

X is OH, R<sub>2</sub> is NH<sub>2</sub>, R<sub>5</sub> is CH<sub>2</sub>OH, R<sub>6</sub> is H, and R<sub>1</sub> is C<sub>6</sub> alkoxy, OCH<sub>2</sub>cyclopropyl, OCH<sub>2</sub>cyclopentyl, O-(2,2,3,3-tetrafluoro-cyclobutyl), OCH<sub>2</sub>CHF<sub>2</sub>, (5-indanyl)oxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>5</sub>, or C<sub>6</sub> alkylamino, (R) or (S)-sec-butylamino, C<sub>5</sub> cycloalkylamino, exo-norbornane amino, N-methyl-N-isoamylamino, phenylamino with a fluoro substituent, a C<sub>2</sub> sulfone group, a C<sub>7</sub> alkyl group, a cyano group, a CONH<sub>2</sub> group, or 3,5-dimethylphenyl; or

X is H, R<sub>2</sub> is NH<sub>2</sub>, R<sub>5</sub> is CH<sub>2</sub>OH, R<sub>6</sub> is H, and R<sub>1</sub> is *n*-hexyloxy.

78. (new) A compound selected from the group consisting of compound numbers 2, 3, 5, 7-25, 28, 29, 31-33 and 35-40 as defined below, or a pharmaceutically acceptable salt of such a compound:

Applicant: Martyn Pritchard et al. Serial No.: 10/598,520 Attorney's Docket No.: 13425-0200US1 / BV-1093 US

Filed : December 7, 2007

Page : 17 of 36

| X OH               |    |   |
|--------------------|----|---|
| Compound<br>Number | X  | $\mathbf{R_1}$  |
| 2                  | ОН | OCH <sub>2</sub> CHF <sub>2</sub>   |
| 3                  | ОН | OCH <sub>2</sub> cyclopropyl  |
| 5                  | ОН | O CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> |
| 7                  | OH | O-(4-cyano)Ph   |
| 8                  | ОН | O-(3-Ph)Ph  |
| 9                  | ОН | O-(2,5-F <sub>2</sub> )Ph   |
| 10                 | ОН | O-(2,4-F <sub>2</sub> )Ph   |
| 11                 | ОН | O-(3,4-F <sub>2</sub> )Ph   |
| 12                 | ОН | O-(2,3,5-F <sub>3</sub> )Ph   |
| 13                 | ОН | O-(3-Me, 4-F)Ph   |
| 14                 | ОН | O-(2-Me)Ph  |
| 15                 | ОН | O-(3-Br)Ph  |
| 16                 | ОН | O-(4-Me)Ph  |
| 17                 | OH | 5-indanyloxy  |
| 18                 | ОН | O-(3-CH(CH <sub>3</sub> ) <sub>2</sub> )Ph  |
| 19                 | ОН | NHCH <sub>3</sub>   |
| 20                 | ОН | NHCH <sub>2</sub> CH <sub>3</sub>   |
| 21                 | OH | N(CH <sub>3</sub> ) <sub>2</sub>  |
| 22                 | OH | NH-(R)-sec-Butyl  |
| 23                 | ОН | NH-(S)-sec-butyl  |

Serial No.: 10/598,520

December 7, 200718 of 36 Filed

Page

| Compound<br>Number | X  | ${f R_1}$   |
|--------------------|----|---|
| 24                 | ОН | NHCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> |
| 25                 | ОН | NH-exo-norbornane   |
| 28                 | ОН | NH-(4-F)Ph  |
| 29                 | ОН | NH-cyclopentyl  |
| 31                 | ОН | N(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> CH(CH <sub>3</sub> ) <sub>2</sub>              |
| 32                 | ОН | OCH <sub>2</sub> cyclopentyl  |
| 33                 | ОН | SO <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>   |
| 35                 | ОН | O-(2,2,3,3-tetrafluoro-   |
|                    | OH | cyclobutyl)   |
| 36                 | ОН | CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>   |
| 37                 | ОН | 3,5-Me <sub>2</sub> -Phenyl   |
| 38                 | ОН | CN  |
| 39                 | OH | CONH <sub>2</sub>   |
| 40                 | H  | O CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>                 |

79. (new) A compound according to claim 78 selected from the group consisting of compound numbers 2, 3, 5, 7-13, 15, 17-25, 28, 29, 31-33 and 35-40 as defined below, or a pharmaceutically acceptable salt of such a compound:

Applicant: Martyn Pritchard et al. Serial No.: 10/598,520 Attorney's Docket No.: 13425-0200US1 / BV-1093 US

: December 7, 2007 : 19 of 36 Filed

Page

| Compound | X  | $\mathbf{R_1}$   |
|----------|----|--|
| Number   |    |  |
| 2        | OH | OCH <sub>2</sub> CHF <sub>2</sub>  |
| 3        | OH | OCH <sub>2</sub> cyclopropyl   |
| 5        | ОН | O CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>    |
| 7        | OH | O-(4-cyano)Ph  |
| 8        | ОН | O-(3-Ph)Ph   |
| 9        | OH | O-(2,5-F <sub>2</sub> )Ph  |
| 10       | ОН | O-(2,4-F <sub>2</sub> )Ph  |
| 11       | ОН | O-(3,4-F <sub>2</sub> )Ph  |
| 12       | OH | O-(2,3,5-F <sub>3</sub> )Ph  |
| 13       | ОН | O-(3-Me, 4-F)Ph  |
| 15       | ОН | O-(3-Br)Ph   |
| 17       | ОН | 5-indanyloxy   |
| 18       | OH | O-(3-CH(CH <sub>3</sub> ) <sub>2</sub> )Ph   |
| 19       | ОН | NHCH <sub>3</sub>  |
| 20       | ОН | NHCH <sub>2</sub> CH <sub>3</sub>  |
| 21       | ОН | N(CH <sub>3</sub> ) <sub>2</sub>   |
| 22       | ОН | NH-(R)-sec-Butyl   |
| 23       | ОН | NH-(S)-sec-butyl   |
| 24       | ОН | NHCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>    |
| 25       | ОН | NH-exo-norbornane  |
| 28       | ОН | NH-(4-F)Ph   |
| 29       | ОН | NH-cyclopentyl   |
| 31       | OH | N(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> CH(CH <sub>3</sub> ) <sub>2</sub> |
| 32       | OH | OCH <sub>2</sub> cyclopentyl   |
| 33       | OH | SO <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>                                      |
| 35       | OH | O-(2,2,3,3-tetrafluoro-<br>cyclobutyl)   |

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 20 of 36

| Compound<br>Number | X  | $\mathbf{R_1}$  |
|--------------------|----|---|
| 36                 | ОН | CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> |
| 37                 | ОН | 3,5-Me <sub>2</sub> -Phenyl   |
| 38                 | OH | CN  |
| 39                 | OH | CONH <sub>2</sub>   |
| 40                 | Н  | O CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>               |

80. (new) An oral dosage form comprising in said oral dosage form a composition comprising a compound of the following general formula:

$$R_{6}$$
 $R_{1}$ 
 $R_{5}$ 
 $R_{1}$ 

or a pharmaceutically acceptable salt thereof; and a physiologically acceptable carrier, excipient or diluent; and wherein:

X is OH, R<sub>2</sub> is NH<sub>2</sub>, R<sub>5</sub> is CH<sub>2</sub>OH, R<sub>6</sub> is H, and R<sub>1</sub> is C<sub>5</sub>-C<sub>6</sub> alkoxy, OCH<sub>2</sub>cyclopropyl, OCH<sub>2</sub>cyclopentyl, O-(2,2,3,3-tetrafluoro-cyclobutyl), phenoxy, substituted phenoxy, OCH<sub>2</sub>CH<sub>2</sub>OH, or OCH<sub>2</sub>CHF<sub>2</sub>, (5-indanyl)oxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>5</sub>, or C<sub>6</sub> alkylamino, (R) or (S)-sec-butylamino, C<sub>5</sub> or C<sub>6</sub> cycloalkylamino, exo-norbornane amino, N-methyl-N-isoamylamino, phenylamino, phenylamino with either methoxy or fluoro substituents, a C<sub>2</sub> sulfone group, a C<sub>7</sub> alkyl group, a cyano group, a CONH<sub>2</sub> group, or 3,5-dimethylphenyl; or

X is H, R<sub>2</sub> is NH<sub>2</sub>, R<sub>5</sub> is CH<sub>2</sub>OH, R<sub>6</sub> is H, and R<sub>1</sub> is *n*-hexyloxy.

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 21 of 36

81. (new) An oral dosage form according to claim 80, wherein the dosage form is a solid oral dosage form.

- 82. (new) An oral dosage form according to claim 80, wherein the dosage form is a form selected from the group consisting of a tablet and a capsule.
- 83. (new) An oral dosage form according to claim 80, wherein the dosage form is suitable for human administration.
- 84. (new) An oral dosage form according to claim 80, wherein the compound is present in the dosage form at a dose that gives rise to a peak plasma concentration of the compound that is less than the EC<sub>50</sub> value of the compound at adenosine receptors at pH 7.4 following administration of the dosage form to a human.
- 85. (new) An oral dosage form according to claim 80, wherein the compound is present in the dosage form at a dose that results in a peak plasma concentration of the compound that is one ten thousandth to one half of the lowest EC<sub>50</sub> value of the compound at adenosine receptors at pH 7.4 following administration of the dosage form to a human.
- 86. (new) An oral dosage form according to claim 80, wherein the compound is present in the dosage form at a dose that results in a plasma concentration of the compound being maintained for more than one hour that is one ten thousandth to one half of the lowest EC50 value of the compound at adenosine receptors at pH 7.4 following administration of the dosage form to a human.
- 87. (new) An oral dosage form according to claim 80, wherein the compound is present in the dosage form at a dose that results in a peak plasma concentration of the compound that is one ten thousandth to one half of the lowest Kd of the compound at adenosine receptors at pH 7.4 following administration of the dosage form to a human.
- 88. (new) An oral dosage form according to claim 80, wherein the compound is present in the dosage form at a dose that results in a plasma concentration of the compound being

Serial No.: 10/598,520

Filed: December 7, 2007

Page : 22 of 36

maintained for more than one hour that is one ten thousandth to one half of the lowest EC50 value of the compound at adenosine receptors at pH 7.4 following administration of the dosage form to a human.

- 89. (new) An oral dosage form according to claim 80, wherein the compound is present in the dosage form at a dose that is one ten thousandth to one half of the minimum amount of the compound that gives rise to bradycardia, hypotension or tachycardia side effects following administration of the dosage form to a human.
- 90. (new) An oral dosage form according to claim 80, wherein the compound is present in the dosage form at a dose that is one thousandth to one half of the minimum amount of the compound that gives rise to bradycardia, hypotension or tachycardia side effects following administration of the dosage form to a human.
- 91. (new) An oral dosage form according to claim 80, wherein the compound is present in the dosage form at a dose that is one hundredth to one half of the minimum amount of the compound that gives rise to bradycardia, hypotension or tachycardia side effects following administration of the dosage form to a human.
- 92. (new) An oral dosage form according to claim 80, wherein the compound is present in the oral dosage form in an amount of less than 28mg.
- 93. (new) An oral dosage form according to claim 80, wherein the compound is present in the oral dosage form in an amount of 0.07 to 28mg.
- 94. (new) An oral dosage form according to claim 80, wherein the compound is present in the oral dosage form in an amount of 0.7 to 7mg.